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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/312,351

05/14/1999

JON A. WOLFF

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03/25/2005

MIRUS CORPORATION
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EXAMINER

WOITACH, JOSEPH T

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/312,351

Applicant(s)

WOLFF ET AL.

Examiner

Joseph T. Woitach

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-11 and 19-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-11 and 19-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

This application claims benefit to provisional application 60/085,764, filed May 16, 1998.

The amendment filed March 17, 2003, has been received and entered. The specification was amended.

Applicants' amendment filed January 4, 2005 has been received and entered. Claims 1-6, 12-18 have been canceled. Claims 7-11 and 24 have been amended. Claims 7-11, 19-28 are pending and currently under examination.

Specification

The nucleotide sequence disclosure contained in this application fails to comply with 37 CFR 1.821-1.825 because the declaration that the sequence listing and that contained on the CRF are the same has not been provided.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-11, 24-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Initially, it is noted that the amendment to the claims have addressed the previous basis of rejection.

It is noted that claim 7 has been amended to recite a composition comprising “a disulfide bond located between at least two reactive groups, that have reacted to form covalent bonds with different molecules on each side of the disulfide bond”. The metes and bounds of the claim are indefinite because it is unclear if the reactive groups are still present or have been lost when they reacted. Further, with a pseudo-product by process description of the composition, the chemical nature of the final product and exactly what has to be present to meet the limitations of the claims is not clearly set forth. Moreover, “reactive groups” is indefinite because it can only be determined relative to another compound under specific conditions, i.e. one compound may be reactive under one buffer condition, but not another, or be able to react to one class of compounds but not another. It is unclear if a group is capable of reacting with anything if it would be considered reactive, thus encompassing any chemical compound because there is another compound under the proper conditions that will react with the chemical compound. It is noted that review of the present specification the term “reactive groups” is not defined in the present specification. Similarly with claim 24, it is unclear what the term “reactable groups” encompasses, and whether they are required in the composition or were only present in the construction of the final product. Dependent claims set forth other general characteristics of the compound as a whole, however fail to clarify the nature of the reactive groups, nor the requirement or absence from the claimed composition.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Specifically, claim 24 has been amended to recite "that is activated by intramoleculr attack from a free thiol such that it is cleaved more rapidly than oxidized glutathione", however literal support for this phrase can not be found in the present specification. Review of the teachings of the specification does not indicate that among the potential R groups that a third sulfhydryl group was contemplated. Further, it is not taught where this is present to provide the particular property claimed.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 24-28 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. As noted above, there is no specific description nor guidance to what this phrase encompasses, nor how to generate this compound. Further, if a third thiol group existed in the composition for intramolecular attack that would result in a rapid cleavage of a disulfide bond, it is unclear how such a chemical would be made or exist in light of this property.

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MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-11, 19-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Pierce catalog as evidenced by Arpicco *et al.*

Assessing what is required and encompassed by the present independent claims it appears that all that is required is a compound with a di-sulfide bond that is cleaved more rapidly that

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oxidized glutathione. The exact nature of the chemical composition on either side of the disulfide bond is unclear, but is being interpreted to encompass at least anything that does not affect the ability of the di-sulfide bond to be cleaved more rapidly than glutathione. Claims 24-28 are included in the basis of the rejection because while they appear to require the presence of a third sulfhydryl group it is unclear when it was present or if it has to be present in the final product since it was "activated" (claim 24).

The Pierce catalog discloses multiple bi-functional and hetero-bi-functional cross linkers that contain disulfide bonds (pages T-157-T-200). As evidence by Arpicco *et al.* the disulfide bonds of these compounds are more labile and are cleaved more rapidly than glutathione. In light of the minimum requirement that the claimed composition must have a di-sulfide bond that is cleaved more rapidly than glutathione and any other chemical on either side that does not affect this cleavage rate, the hetero-bi-functional cross-linkers anticipate the claims. Since the compounds disclosed by Pierce were synthesized, and thus imply reactable groups were present, they meet the limitations of the claim to encompass reacted groups. To the extent that the composition still has reactive groups, it is noted that the cross-linkers in Pierce are sold for use in cross-linking additional molecules and maintain different reactive groups on either side of the disulfide bond. Again, because the linker was synthesized the presence of the reactive groups implies that other reactive groups were present/used in the synthesis of the final product.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

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Soukup *et al.* Bioconjug Chem.6(1):135-8. (1995) "Preparation of oligonucleotide-biotin conjugates with cleavable linkers" provides evidence that heterobifunctional cross-linkers were used to link polynucleotides to other molecules, such as biotin.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

Joe Woitach
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